Via Electronic Submission to CompoundingSL@usp.org

November 20, 2018

Ronald T. Pervincenzi, Ph.D
Chief Executive Officer
United States Pharmacopeial Convention
12601 Twinbrook Parkway
Rockville, Maryland 20852-1790

Re: Chapter <797> Pharmaceutical Compounding – Sterile Preparations

Dear Dr. Piervincenzi:

The American Society of Clinical Oncology (ASCO) is pleased to submit these comments on proposed revisions to the U.S. Pharmacopeial Convention (USP) General Chapter <797> Pharmaceutical Compounding – Sterile Preparations. ASCO is the national organization representing over 45,000 physicians and other healthcare professionals specializing in cancer treatment, diagnosis, and prevention. ASCO members are dedicated to conducting research that leads to improved patient outcomes and ensuring that evidence-based practices for the prevention, diagnosis, and treatment of cancer are available to all Americans.

ASCO is deeply committed to ensuring patient and workplace safety through the proper and accurate preparation, handling, and administration of anticancer drug regimens. In 2013, ASCO, along with the Oncology Nursing Society (ONS), released an updated set of chemotherapy administration safety standards that focus on patient protection. Additionally, ASCO has convened a Task Force on Safe Handling of Chemotherapy to develop recommendations for updated safety standards focused on worker and patient protection from exposure to hazardous drugs. In November 2015, ASCO and the National Institutes for Occupational Safety and Health (NIOSH) convened a multi-stakeholder workshop to address issues surrounding the safe handling of hazardous drugs. Recently, ASCO authored a paper addressing some of the most controversial issues related to the safe handling of anticancer drugs.

Although we commend the USP panel and staff for retaining the exclusion under this draft of USP <797> for conventionally manufactured sterile products (see lines 8 through 12), there are important clarifications and edits necessary before the USP panel finalizes this draft. In the absence of our recommended clarifications (described below), the proposed chapter is likely to create unnecessary confusion, interfere with patient access to the administration of life-saving drugs, and undermine the requirements and drug approvals promulgated by the U.S. Food and Drug Administration (FDA).
Moreover, there is an alarming trend in which the USP panels have promulgated draft and final policies in the areas of safe handling and compounding without incorporating important recommendations from the community of medical oncologists to adequately account for the day-to-day operations of modern oncology practices. We have important insights regarding the scientific basis, clinical impacts, and practical aspects of caring for individuals with oncology in various practice settings. We strongly urge the USP panel to adopt our recommendations.

In particular, the USP panel should include the language for conventionally manufactured sterile products (lines 8 to 12) in the final version of the USP <797>. However, we strongly recommend that the panel amend this language in two important ways.

First, the language at lines 8 to 12 should be amended to harmonize USP <797> with the definition of compounding used by the FDA as enacted by Congress. Section 503A of the Federal Food, Drug, and Cosmetic Act excludes the following activities from the definition of compounding: “…mixing, reconstituting, or other such acts that are performed in accordance with directions contained in approved labeling provided by the product’s manufacturer and other manufacturer directions consistent with that labeling.” As such, lines 8 to 12 of USP <797> should be amended to include explicit reference to “other manufacturer directions” to bring this provision more closely in line with the FDA definition of compounding.

Second, to harmonize USP <797> with the definition of compounding used by the FDA and to avoid interfering with labeling that is FDA-approved for the administration of anticancer drugs, we urge the USP <797> panel to amend the language in lines 8 and 12 to clarify that the exclusion for conventionally manufactured sterile products applies to both non-hazardous and hazardous drugs. Comments made during the open microphone session in September have already created significant concern and confusion regarding the interpretation of the language in lines 8 to 12 with other parts of the introduction.

Based on the discussion above, lines 8 through 12 of the proposed chapter should be revised to read as follows:

“Preparing a conventionally manufactured sterile product, including both non-hazardous and hazardous drugs, in accordance with the directions contained in approved labeling provided by the product’s manufacturer or with directions provided by the manufacturer consistent with such labeling is not compounding as long as the product is prepared for an individual patient and follows the provisions for administration below.”

In addition, the USP panel should amend lines 13 through 16 to eliminate the concept of immediacy from within the definition of “administration.” The draft chapter’s definition of administration reads “the direct and immediate application of a conventionally manufactured product or a CSP to a patient by injecting, infusing or otherwise providing a sterile medication in its final form” (emphasis added).

The concept of immediacy should be eliminated from the definition of administration. Administration should fall outside of USP <797>, and using terms such as “immediate” will create confusion and will have adverse impacts on the ability of oncology practices throughout the United States to administer...
anticancer drug regimens. The reference to “immediate” administration is arbitrary and is not well-grounded in science, and in non-emergency situations, immediate administration is not necessary.

Differences in the setting of care, conventionally manufactured sterile preparations, CSPs or other factors may all influence how quickly is reasonable within the course of preparation and administration by health care professionals. For example, physician practices may prepare their conventionally manufactured products on the morning of the administration date and store them for short periods of time in a manner that is consistent with best practices, clinical care, and the timeframes and storage instructions provided by the manufacturer.

For the reasons described above, the panel would better serve the public by removing the phrase “and immediate” from lines 13 to 16.

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Thank you for the opportunity to provide comments on the revised draft chapter of USP <797>. If we can provide any information or expertise on issues involving hazardous drugs or other aspects of the operation of modern oncology practices, please contact Jennifer Brunelle at Jennifer.Brunelle@asco.org.

Sincerely,

Monica Bertagnolli, MD, FACS, FASCO
President, American Society of Clinical Oncology